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THE TREATMENT OF THE HYPOTENSIVE STATE ACCOMPANYING MYOCARDIAL INFARCTION

The progress made in recent years in the management of myocardial infarction has been in the treatment of arrhythmias and congestive failure, in accuracy of diagnosis, and in the prevention of thrombo-embolic complications. The treatment of shock accompanying myocardial infarction has been highly controversial. An important cause of death within the first 24 to 48 hours after coronary occlusion is profound hypotension and the development of shock. This state occurs in approximately 10 per cent of all cases of myocardial infarction,[1] and is associated with a mortality rate which is high, 80 to 90 per cent.[2,3] Since the total mortality rate following acute myocardial infarction is 20 per cent,*[1] the shock state occurs in 40 to 45 per cent of those patients who die.

During the acute stage of myocardial infarction, transient moderate hypotension is frequent and is usually considered salutary. However, if the blood pressure falls to a critical level for a sufficient time, the clinical picture of shock supervenes, and the prognosis becomes grave. The shock state is considered to exist when the systolic blood pressure falls abruptly and remains below an arbitrary level of 80 to 90 mm Hg., for at least one hour.[1,3,5] (In previously hypertensive patients, shock may occur at a higher pressure (100 mm Hg.)). During this time classic signs of circulatory collapse appear, viz., rapid pulse (sinus tachycardia), small pulse pressure, poor heart sounds, gallop rhythm, pallid cyanosis, faintness, weakness, cold moist skin, and stupor or coma.

*The Committee on Anticoagulants of the American Heart Association[4] reported a mortality of 16 per cent and excluded those who died within the first 24 hours.

ETIOLOGY

The etiology of shock accompanying myocardial infarction is still obscure. Although shock with myocardial infarction may produce a clinical picture similar to that of traumatic or hemorrhagic shock, the greatest etiologic difference is the initiating cardiac insult present in the former. After coronary occlusion a significant portion of the ischemic ventricular myocardium is deleted within a few minutes,[6,7,8] thereby throwing the burden of ventricular work on the remaining muscle. Hypodynamic contractions and cardiac dilatation may supervene unless full compensatory reactions of the remaining fractions are brought into play.[7] If sufficient myocardium survives, dynamics return to normal, with restoration of adequate cardiac output and circulatory balance.

As a consequence of reduced cardiac output,[9,10] and perhaps other, less known factors, a severe reduction in systemic blood pressure may ensue during the period of hypodynamic contractions. The coronary blood flow and collateral intercoronary anastomoses are thereby reduced.[8] The resultant myocardial depression[11] contributes further to the circulatory failure. Experimentally, hypotension increases the area of ballooning produced by coronary occlusion.[8] Furthermore, when blood pressure is lowered in a dog with a constricted but not occluded coronary artery, contractility ceases in the area supplied by that artery. After restoration of the blood pressure, normal contractility returns. Clinically, patients with coronary arteriosclerosis may develop subendocardial infarcts as a result of hemorrhage. Likewise in patients with generalized coronary arteriosclerosis and acute coronary occlu-

ANNUAL MEETING

The Annual Meeting and Twenty-Fifth Scientific Sessions of the American Heart Association will be held at the Hotel Statler, Cleveland, Ohio, April 18-20, 1952. All of those planning to attend should make room reservations directly with the Hotel Statler in Cleveland at the earliest possible date.

sion, hypotension from whatever cause, produces significant ischemia in large segments of myocardium supplied by the stenotic coronary arteries. Efforts to increase systemic blood pressure are indicated.

Diminished cardiac output is a consistent finding in shock with infarction. Blood and plasma volume are not immediately reduced, but later reduction may be the result of dehydration due to sweating or vomiting.[12] The degree of reduction of circulating blood volume per se is insufficient to produce the picture of shock.[13] Usually there is no evidence of failure of the right ventricle. The peripheral and central venous pressures are not elevated. However, in a majority of patients [and in experimental occlusion in dogs[14]] there is some indication of incompetence of the left ventricle. There is evidence of elevation of left atrial and pulmonary venous pressures: pulmonary congestion, rales, and prolonged circulation time.[15,16] Since venous return of the left ventricle is more than adequate, the fall in cardiac output with resultant shock cannot be attributed to the mechanisms that are thought to be important in traumatic shock. The predominant involvement of the left ventricle in myocardial infarction with relative competence of the right ventricle readily explains these changes. Congestive heart failure frequently accompanies shock in acute infarction, particularly when the patient previously had suffered from congestive failure or loss of cardiac reserve.[1,5,13] In such patients increasing signs of congestion may predominate over those of shock.

Other factors contributory to the maintenance or initiation of shock include excessive sedation, cardiogenic reflexes, pain and anxiety, acidosis, tachycardia (of ventricular or supraventricular origin), auricular fibrillation with rapid ventricular rate, hemorrhage, and concomitant intravascular thrombosis.

In summary, shock accompanying myocardial infarction is (1) a manifestation of forward heart failure[17] due to deletion of significant portions of myocardium, (2) characterized by reduced cardiac output, hypotension, reduced general coronary flow and collateral intercoronary anastomosis, and (3) is aggravated by peripheral factors.

THERAPY

Despite the universally grave prognosis of shock accompanying myocardial infarction, specific therapy remains ill-defined. In fact, antishock therapy has even been discouraged by some,[18,19] on the basis that low blood pressure relieves the work of the heart. This may be true in mild hypotension without signs of shock. However, prolonged severe hypotension with failure of perfusion of vital organs results in an irreversible state of shock.

All measures designed to combat shock in myocardial infarction should be directed toward supporting the *uninfarcted* muscle. The objective of therapy is to restore the effective head of blood pressure in the aorta to perfuse adequately the coronary, cerebral, renal, hepatic, and other vital circulations. As far as the heart is concerned, elevation of the blood pressure (to 100 mm systolic in patients who were previously normotensive, and 120 mm in those previously hypertensive) improves the total coronary circulation, enhances the chances of survival of borderline myocardium and that supplied by stenotic arteries, and may decrease the size of the infarct. In many patients, the area of ischemic myocardium is relatively so large that death is inevitable regardless of the treatment. Similarly, there are some with moderate hypotension who recover without specific medication. Between these two extremes, there are many patients in whom the treatment of shock may be lifesaving.[1,13]

Specific therapy includes the use of (1) pressor amines, (2) transfusion, (3) digitalis glycosides, and (4) venesection.

VASOPRESSOR DRUGS

The most rational therapy at the present time appears to be the use of vasopressor drugs and cardiac stimulants.[1,8,13] The ideal pressor drug would elevate blood pressure, increase peripheral resistance, produce a proportionate increase of coronary flow, have minimal side effects, and would not decrease cardiac output or produce serious arrhythmias. Although the ideal pressor drug has not been identified as yet, some amines now available fulfill most of these requirements. These include nor-epinephrine, mephentermine, desoxyephedrine, ephedrine, paredrine, neosynephrine and amphetamine. Objections are justifiably raised to the use of epinephrine which enhances the irritability of the myocardium sufficiently to produce serious ectopic rhythms. Most of the above named amines have a greater safety range than epinephrine since they are capable of producing the same level of blood pressure without inducing ventricular arrhythmias. All sympathetic amines in sufficiently large doses will produce ectopic rhythms. The metabolic effects of sympathetic amines consist of an increase of general and cardiac metabolism, and an anoxating effect on the myocardium.[20] The above amines have a lesser tendency to stimulate metabolism.[13] Although the anoxating effect is out of proportion to the increase of coronary flow, the elevation of systemic blood pressure and coronary flow probably outweigh the apparent disadvantages. Large increases of coronary flow may occur without significant changes in heart rate or aortic pressure.[21] With the elevation of aortic pressure there is further augmentation of basic coronary flow.

The pressor amines can be used easily and safely. A definite pressor response is usually achieved rapidly without introducing complicating factors such as those associated with alteration of blood volume. Recently encouraging results have been reported with sympathetic amines.[1,8,22] Seventeen patients in shock associated with myocardial infarction were recently treated with mephentermine.[1*] Thir-

*Supplied by Wyeth, Inc., Philadelphia, Pa. (Wyamine)

teen patients survived the episode of shock. Seven were eventually discharged from the hospital, and six succumbed to secondary complications from 2 to 26 days after treatment. A significant pressor response was obtained in sixteen of the seventeen patients.

METHOD OF ADMINISTRATION OF SYMPATHETIC AMINES

Initially, the intravenous route is indicated in view of the decreased peripheral circulation and poor absorption. Five to fifteen milligrams of mephentermine or ephedrine may be given intravenously. This usually produces an immediate pressor response. To sustain this gain, 35-70 mgm are diluted in 100 ml. of 5 per cent glucose in water, and administered slowly over the next 2 hours, the rate of flow being regulated to maintain this rise without attaining an excessively high pressure. Frequent pulse rate and blood pressure determinations and direct recording electrocardiographic tracings are advised. Usually the patient improves clinically as the blood pressure rises. Occasionally one intravenous injection suffices to raise the blood pressure to a critical level which once reached is maintained without further pressor therapy. Intramuscular depot injections of 25 mgm every one to two hours may be needed to maintain the blood pressure. Generally with this regime the heart rate will change less than ten per cent. Neosynephrine (5 mgm) or epinephrine (3-4 minims of 1:1000) may be given every fifteen to thirty minutes when other amines are not readily available.

TRANSFUSIONS

Recent reports[3,5,8,23] indicate some benefit from blood and plasma transfusions, particularly if given early, especially in the absence of a high initial venous pressure. However, in the absence of evidence of diminished circulating blood volume, the rationale of transfusion may be dubious. Nevertheless in eight of the eleven patients who improved the blood pressure rose during transfusion despite the presence of congestive heart failure, indicating that some patients respond to augmented cardiac filling with an increase in cardiac output or peripheral resistance.[3]

METHOD OF ADMINISTRATION

Whole blood or plasma transfusions have been given in successful cases at a rate of 2-4 ml. per minute with an average of 200 ml. per hour.[3,5,8] The range of the rate of administration has varied from 60 to 500 ml. per hour. The rate of transfusion must be watched carefully to prevent acute pulmonary edema. The transfusion should be terminated if increasing signs of congestive failure appear. On the other hand, the rate of administration should be increased if signs of overloading are absent and if the blood pressure remains low or falls.[5] Plasma is the fluid of choice if there is hemoconcentration due to vomiting, excessive sweating and inanition. In the presence of severe anemia, whole blood is indicated. Intravenous fifty per cent glucose is rarely effective.

The results of transfusion have not been striking. Although eleven of thirty patients improved, Epstein and Relman[3] could not demonstrate statistical benefit from transfusion. Sampson and Singer[5] reported recovery in one of eleven patients, and later three of six additional cases. The usefulness of transfusion is limited by the slow pressure response which is less striking than that of sympathetic amines, and by the complications of pulmonary edema which may occur despite constant observation. In myocardial infarction due to severe anemia (acute blood loss in bleeding ulcer or trauma) transfusion may be lifesaving.

Retrograde arterial transfusion: The use of retrograde arterial transfusion has been suggested[24] to elevate the coronary perfusion pressure more acutely, and to avoid the time lag which occurs in venous transfusion. As yet no reports have been made with this promising technique.

DIGITALIS GLYCOSIDES

The use of digitalis glycosides, particularly the rapidly acting ones (strophanthin, ouabain, digoxin, etc.) is valid[16] particularly since there is evidence of congestive failure even in patients with predominant signs of shock. Strophanthin increases cardiac output, efficiency and peripheral blood pressure within a few minutes.[25] The danger of enhancing ventricular irritability and thus producing ventricular fibrillation is present only with excessive amounts.[26] Likewise, cardiac rupture is unlikely since this complication occurs from the fourth to seventh day, and shock usually occurs earlier.

Method of administration: In patients who have not previously received digitalis glycosides, the usual dose of 0.25 to 0.50 mgm of strophanthin or ouabain is administered over five measured minutes. Pressor drugs may be combined with this therapy. Because of the rapid excretion, longer acting digitoxin or digitalis should be started within six hours, so that within the next 24 hours, a calculated saturating dose of the latter drugs has been given.

VENESECTION

Venesection or application of venous tourniquets* is indicated in preference to transfusion, for patients in shock with frank congestive failure and pulmonary edema.[16] The pulmonary edema may be a greater threat than the shock. However, routine venesection in the absence of pulmonary edema cannot be recommended until further observations have been reported.

GENERAL REMARKS ABOUT THERAPY

Good nursing care and immediate supervision of therapy by the attending physician are required in

*The employment of tourniquets on the extremities is a satisfactory substitute for venesection but the danger of peripheral venous thrombosis usually contraindicates this method for prolonged use.

the cautious elevation of the blood pressure and its maintenance. Oxygen inhalation, reassurance, shock position, supportive drugs such as coramine and caffeine, and adequate sedation are valuable adjuncts.

Differential diagnosis: Other specific causes of hypotension in patients with myocardial infarction must be excluded. Tachycardia of ventricular or supraventricular origin may simulate this condition, and should be confirmed electrocardiographically. Prompt appropriate intravenous therapy usually will restore the mechanism and terminate the hypotension due to the rapid heart rate. If the blood pressure remains low after conversion, peripheral vasopressor drugs are indicated. Shock may also be produced by internal or external hemorrhage in patients with coronary arteriosclerosis. The clinical picture will be confused further by electrocardiographic changes of infarction or ischemia, usually subendocardial. Whole blood transfusion and treatment of the underlying cause are necessary.

Indications for various types of therapy and their combination: If the patient is moderately hypotensive, asymptomatic and without signs of circulatory collapse, no specific therapy is indicated. However, continuous observation is advisable. Once shock appears, immediate treatment should be started. If there is no elevation of venous pressure and no pulmonary congestion, pressor drugs are preferred. If repeated intravenous injections do not sustain the blood pressure above 100 mm Hg., whole blood or plasma (less than 250 cc per hour) should be given within one hour. The presence of shock and congestive failure is an indication for rapid digitalization, followed when necessary by peripheral vasopressor drugs. In mild failure, transfusion may be administered cautiously. However, in fulminating pulmonary edema, transfusion is contraindicated and venesection (250-500 cc) is the treatment of choice. If shock and tachycardia of ventricular or supraventricular origin are present, specific therapy against the tachycardia is first indicated.

Causes of death and failures in treated cases: Insufficient surviving myocardium and delay in instituting anti-shock therapy are responsible for the high mortality. Some patients recover from shock but suffer from the consequence of prolonged hypotension, i.e., lower nephron nephrosis, hepatic insufficiency, and spontaneous intravascular thrombosis in the brain, extremities, mesentery or other organs. Other complications include secondary myocardial infarction, extension of the original thrombus, congestive heart failure, and arrhythmias.

SUMMARY

The treatment of shock due to coronary thrombosis and myocardial infarction rests on a firm clinical basis. There is need for vigorous early treatment to restore an effective head of blood pressure. Sympathetic pressor amines, strophanthin, judicious use of transfusions, and supportive therapy have yielded encouraging results. Treatment must be individualized, often combining various forms of therapy.

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